A New Tool for Aligning Assay Endpoints to Adverse Outcome Pathways

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A critical challenge to the implementation of non-animal approaches in chemical safety testing is linking endpoints measured in these approaches to adverse physiological responses in vivo. The adverse outcome pathway (AOP) framework allows these molecular, cellular, and tissue-level endpoints to be placed in a biologically relevant context. The National Toxicology Program's Integrated Chemical Environment (ICE) web resource houses curated data from in vivo, in vitro, and in silico endpoints. A new feature of ICE maps assay endpoints to key events within AOPs. This feature can be used to identify data gaps and build confidence in mechanistic plausibility and relevance. This new ICE feature enables use of ICE with AOPXplorer, a Cytoscape plugin that allows visualization of data in AOP networks to build confidence in the mechanistic plausibility and relevance of a proposed defined approach. Our presentation will use the skin sensitization AOP and putative AOPs for androgen and estrogen receptor pathways to demonstrate the utility of this feature. This was funded with U.S. federal funds from the NIEHS/NIH/HHS under Contract HHSN273201500010C.